```
=> d his

     (FILE 'HOME' ENTERED AT 12:45:47 ON 02 NOV 2006)

     FILE 'CAPLUS' ENTERED AT 12:46:03 ON 02 NOV 2006
L1             0 S CHITOSAN(10A)ALKYLSULFONATED
L2            62 S CHITOSAN(10A)SULFONATED
L3             5 S L2(L)(ANTIBACTERIA? OR BACTERIA? OR ANTIMICROBIA? OR MICROBIA

     FILE 'REGISTRY' ENTERED AT 14:10:34 ON 02 NOV 2006
               E SOPHOROLIPID/CN

     FILE 'CAPLUS' ENTERED AT 14:11:10 ON 02 NOV 2006
L4           155 S SOPHOROLIPID#
L5             2 S L4(L)(SEPSIS OR SEPTIC)

     FILE 'MEDLINE, EMBASE, BIOSIS' ENTERED AT 14:12:17 ON 02 NOV 2006
L6             6 S L5
```

=> d ibib abs 1-2

L5 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1347078 CAPLUS
DOCUMENT NUMBER: 144:305055
TITLE: Sophorolipids block lethal effects of septic shock in rats in a cecal ligation and puncture model of experimental sepsis
AUTHOR(S): Bluth, Martin H.; Kandil, Emad; Mueller, Catherine M.; Shah, Vishal; Lin, Yin-Yao; Zhang, Hong; Dresner, Lisa; Lempert, Leonid; Nowakowski, Maja; Gross, Richard; Schulze, Robert; Zenilman, Michael E.
CORPORATE SOURCE: SUNY Downstate Medical Center, Department of Surgery, National Science Foundation Center for Biocatalysis and Bioprocessing of Macromolecules, Polytechnic University, Brooklyn, NY, USA
SOURCE: Critical Care Medicine (2006), 34(1), 188-195
CODEN: CCMDC7; ISSN: 0090-3493
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: Sophorolipids, a family of natural and easily chemoenzymically modified microbial glycolipids, are promising modulators of the immune response. The potential of the therapeutic effect of sophorolipids was investigated in vivo in a rat model of sepsis and in vitro by anal. of nitric oxide and cytokine production Design: Prospective, randomized animal study. Setting: Exptl. laboratory Subjects: Male Sprague-Dawley rats, 200-240 g. Interventions: Intra-abdominal sepsis was induced in vivo in 166 rats via cecal ligation and puncture (CLP); 60 rats were used to characterize the model. The remaining rats were treated with sophorolipids or vehicle (dimethylsulfoxide [DMSO]/physiol. saline) by i.v. (iv) tail vein or i.p. (IP) injection immediately post-CLP (25/group). Survival rates were compared at 36 h after surgery. In vitro, macrophages were cultured in lipopolysaccharide (LPS) ± sophorolipid and assayed for nitric oxide (NO) production and gene expression profiles of inflammatory cytokines. In addition, splenic lymphocytes isolated from CLP rats ± sophorolipid treatment (three per group) were analyzed for cytokine production by RNase protection assay. Measurements and main results: CLP with 16-gauge needles optimized sepsis induction and resultant mortality. Sophorolipid treatment improved rat survival by 34% (iv) and 14% (IP) in comparison with vehicle controls ($p < .05$ for iv treatment). Sophorolipids decreased LPS-induced macrophage NO production by 28% ($p < .05$). mRNA expression of interleukin (IL)-1β was downregulated by 42.5 ± 4.7% ($p < .05$) and transforming growth factor (TGF)-β1 was upregulated by 11.7 ± 1.5% ($p < .05$) in splenocytes obtained 6 h postsophorolipid treatment. LPS-treated macrophages cultured 36 h with sophorolipids showed increases in mRNA expression of IL-1α (51.7%), IL-1β (31.3%), and IL-6 (66.8%) ($p < .05$). Conclusions: Administration of sophorolipids after induction of intra-abdominal sepsis significantly decreases mortality in this model. This may be mediated in part by decreased macrophage NO production and modulation of inflammatory responses.

L5 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:905607 CAPLUS
DOCUMENT NUMBER: 141:355428
TITLE: Treatment and prophylaxis of sepsis and septic shock with sophorolipids
INVENTOR(S): Gross, Richard A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 10 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004214795	A1	20041028	US 2004-807961	20040324
WO 2005094268	A2	20051013	WO 2005-US10060	20050324

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-457070P P 20030324
US 2004-807961 A2 20040324

AB A composition for the prophylaxis or treatment of humans or animals for septic shock and sepsis using a mixture of sophorolipids is disclosed. The in vivo expts. demonstrated that sophorolipids have a protective effect against ongoing endotoxic shock. I.p. injection of sophorolipids 1.5 h after galactosamine-LPS treatment resulted in 53% lower mortality than that observed among pos. control mice.

=> FIL MEDLINE EMBASE BIOSIS

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	12.25	57.38

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.50	-5.25

FILE 'MEDLINE' ENTERED AT 14:12:17 ON 02 NOV 2006

FILE 'EMBASE' ENTERED AT 14:12:17 ON 02 NOV 2006

FILE 'BIOSIS' ENTERED AT 14:12:17 ON 02 NOV 2006

=> s l5
L6 6 L5

=> d ibib abs 1-6

L6 ANSWER 1 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2005693126 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16374148
TITLE: Sophorolipids block lethal effects of septic shock in rats in a cecal ligation and puncture model of experimental sepsis.
AUTHOR: Bluth Martin H; Kandil Emad; Mueller Catherine M; Shah Vishal; Lin Yin-Yao; Zhang Hong; Dresner Lisa; Lempert Leonid; Nowakowski Maja; Gross Richard; Schulze Robert;

Zenilman Michael E
CORPORATE SOURCE: SUNY Downstate Medical Center, Department of Surgery, Brooklyn, NY 11203, USA.. martin.bluth@downstate.edu
SOURCE: Critical care medicine, (2006 Jan) Vol. 34, No. 1, pp. 188-95.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 30 Dec 2005
Last Updated on STN: 21 Jan 2006
Entered Medline: 20 Jan 2006

AB OBJECTIVE: Sophorolipids, a family of natural and easily chemoenzymatically modified microbial glycolipids, are promising modulators of the immune response. The potential of the therapeutic effect of sophorolipids was investigated in vivo in a rat model of sepsis and in vitro by analysis of nitric oxide and cytokine production. DESIGN: Prospective, randomized animal study. SETTING: Experimental laboratory. SUBJECTS: Male Sprague-Dawley rats, 200-240 g. INTERVENTIONS: Intra-abdominal sepsis was induced in vivo in 166 rats via cecal ligation and puncture (CLP); 60 rats were used to characterize the model. The remaining rats were treated with sophorolipids or vehicle (dimethylsulfoxide [DMSO]/physiologic saline) by intravenous (iv) tail vein or intraperitoneal (IP) injection immediately post-CLP (25/group). Survival rates were compared at 36 hrs after surgery. In vitro, macrophages were cultured in lipopolysaccharide (LPS) +/- sophorolipid and assayed for nitric oxide (NO) production and gene expression profiles of inflammatory cytokines. In addition, splenic lymphocytes isolated from CLP rats +/- sophorolipid treatment (three per group) were analyzed for cytokine production by RNase protection assay. MEASUREMENTS AND MAIN RESULTS: CLP with 16-gauge needles optimized sepsis induction and resultant mortality. Sophorolipid treatment improved rat survival by 34% (iv) and 14% (IP) in comparison with vehicle controls ($p < .05$ for iv treatment). Sophorolipids decreased LPS-induced macrophage NO production by 28% ($p < .05$). mRNA expression of interleukin (IL)-1beta was downregulated by 42.5 +/- 4.7% ($p < .05$) and transforming growth factor (TGF)-beta1 was upregulated by 11.7 +/- 1.5% ($p < .05$) in splenocytes obtained 6 hrs postsophorolipid treatment. LPS-treated macrophages cultured 36 hrs with sophorolipids showed increases in mRNA expression of IL-1alpha (51.7%), IL-1beta (31.3%), and IL-6 (66.8%) ($p < .05$). CONCLUSIONS: Administration of sophorolipids after induction of intra-abdominal sepsis significantly decreases mortality in this model. This may be mediated in part by decreased macrophage NO production and modulation of inflammatory responses.

L6 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2005687292 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16374196
TITLE: Sophorolipids in sepsis: antiinflammatory or antibacterial?.
AUTHOR: Napolitano Lena M
SOURCE: Critical care medicine, (2006 Jan) Vol. 34, No. 1, pp. 258-9.
Journal code: 0355501. ISSN: 0090-3493.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Editorial
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 28 Dec 2005
Last Updated on STN: 21 Jan 2006
Entered Medline: 20 Jan 2006

L6 ANSWER 3 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006010951 EMBASE
TITLE: Sophorolipids in sepsis:
Antiinflammatory or antibacterial?.
AUTHOR: Napolitano L.M.
CORPORATE SOURCE: Dr. L.M. Napolitano, Department of Surgery, University of Michigan, School of Medicine, Ann Arbor, MI, United States
SOURCE: Critical Care Medicine, (2006) Vol. 34, No. 1, pp. 258-259.
Refs: 14
ISSN: 0090-3493 CODEN: CCMDC7
COUNTRY: United States
DOCUMENT TYPE: Journal; Editorial
FILE SEGMENT: 004 Microbiology
024 Anesthesiology
037 Drug Literature Index
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jan 2006
Last Updated on STN: 19 Jan 2006
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L6 ANSWER 4 OF 6 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006010904 EMBASE
TITLE: Sophorolipids block lethal effects of septic shock in rats in a cecal ligation and puncture model of experimental sepsis.
AUTHOR: Bluth M.H.; Kandil E.; Mueller C.M.; Shah V.; Lin Y.-Y.; Zhang H.; Dresner L.; Lempert L.; Nowakowski M.; Gross R.; Schulze R.; Zenilman M.E.
CORPORATE SOURCE: Dr. M.H. Bluth, Department of Surgery and Pathology, SUNY Downstate Medical Center, Box 40, 450 Clarkson Avenue, Brooklyn, NY 11203, United States.
martin.bluth@downstate.edu
SOURCE: Critical Care Medicine, (2006) Vol. 34, No. 1, pp. E188.1-E188.8.
Refs: 71
ISSN: 0090-3493 CODEN: CCMDC7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
030 Pharmacology
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jan 2006
Last Updated on STN: 19 Jan 2006
AB Objective: Sophorolipids, a family of natural and easily chemoenzymatically modified microbial glycolipids, are promising modulators of the immune response. The potential of the therapeutic effect of sophorolipids was investigated in vivo in a rat model of sepsis and in vitro by analysis of nitric oxide and cytokine production. Design: Prospective, randomized animal study. Setting: Experimental laboratory. Subjects: Male Sprague-Dawley rats, 200-240 g. Interventions: Intra-abdominal sepsis was induced in vivo in 166 rats via cecal ligation and puncture (CLP); 60 rats were used to

characterize the model. The remaining rats were treated with sophorolipids or vehicle (dimethylsulfoxide [DMSO]/physiologic saline) by intravenous (iv) tail vein or intraperitoneal (IP) injection immediately post-CLP (25/group). Survival rates were compared at 36 hrs after surgery. In vitro, macrophages were cultured in lipopolysaccharide (LPS) ± sophorolipid and assayed for nitric oxide (NO) production and gene expression profiles of inflammatory cytokines. In addition, splenic lymphocytes isolated from CLP rats ± sophorolipid treatment (three per group) were analyzed for cytokine production by RNase protection assay. Measurements and Main Results: CLP with 16-gauge needles optimized sepsis induction and resultant mortality. Sophorolipid treatment improved rat survival by 34% (iv) and 14% (IP) in comparison with vehicle controls ($p < .05$ for iv treatment). Sophorolipids decreased LPS-induced macrophage NO production by 28% ($p < .05$). mRNA expression of interleukin (IL)-1β was downregulated by 42.5 ± 4.7% ($p < .05$) and transforming growth factor (TGF)-β1 was upregulated by 11.7 ± 1.5% ($p < .05$) in splenocytes obtained 6 hrs postsophorolipid treatment. LPS-treated macrophages cultured 36 hrs with sophorolipids showed increases in mRNA expression of IL-1α (51.7%), IL-1β (31.3%), and IL-6 (66.8%) ($p < .05$). Conclusions: Administration of sophorolipids after induction of intra-abdominal sepsis significantly decreases mortality in this model. This may be mediated in part by decreased macrophage NO production and modulation of inflammatory responses.

L6 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:344333 BIOSIS
DOCUMENT NUMBER: PREV200600343465

TITLE: Sophorolipid treatment decreases inflammatory cytokine expression in an in vitro model of experimental sepsis.

AUTHOR(S): Mueller, Cathy M. [Reprint Author]; Lin, Yin-yao; Viterbo, Domenico; Pierre, Joelle; Murray, Shirley A.; Shah, Vishat; Gross, Richard; Schulze, Robert; Zenilman, Michael E.; Bluth, Martin H.

CORPORATE SOURCE: Suny Downstate Med Ctr, Brooklyn, NY 11203 USA

SOURCE: FASEB Journal, (MAR 6 2006) Vol. 20, No. 4, Part 1, pp. A204.
Meeting Info.: Experimental Biology 2006 Meeting. San Francisco, CA, USA. April 01 -05, 2006. Amer Assoc Anatomists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr; Amer Soc Pharmacol & Expt Therapeut.
CODEN: FAJOEC. ISSN: 0892-6638.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 12 Jul 2006
Last Updated on STN: 12 Jul 2006

AB Sophorolipids are a class of membrane-derived glycolipids that have wide ranging potential as treatment in clinical practice. Previous data from our laboratory show that in vivo sophorolipid therapy decreases sepsis related mortality in experimental models. In this study we investigated the effects of sophorolipid treatment on cytokine production in an in vitro model of experimental sepsis . LPS stimulated rat alveolar macrophage cells (NR8383) were cultured in the presence or absence of sophorolipids for 12, 24, 36; and 48 hr. RNA was harvested from each group and assayed for cytokine expression using multiplex PCR. Statistical analyses were performed comparing the LPS treated group (L) with the LPS + sophorolipid treated group (L+S). TNF-a, a proinflammatory cytokine known to play a pivotal role in

septic shock was significantly decreased in the L+S group compared to the L group at 12-24 hr, but trended upward at 36-48hr. Pro-inflammatory cytokines IL-1a and IL-1b followed the same pattern. IL-1 receptor antagonist (RA), which provides a protective effect in experimental sepsis, also showed decreased expression in the L+S compared to L group at 12-24 hr and an upward trend at 36-48hr. Similar expression pattern was found with IL-10, which may affect Th1/Th2 type T cell responses. Sophorolipid treatment decreases expression of important pro-inflammatory cytokines in an in vitro cellular sepsis model and this immunomodulation may be responsible, in part, for sophorolipid mediated decreases in sepsis related mortality. Sophorolipid treatment may delay or prevent sepsis progression by allowing host response immune mechanisms to exert their protective effects.

L6 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2005:529855 BIOSIS
DOCUMENT NUMBER: PREV200510323370
TITLE: Sophorolipid treatment modulates leukocyte adhesion molecule profiles in intra-abdominal sepsis.
AUTHOR(S): Bluth, Martin H. [Reprint Author]; Hardin, Rosemarie; Pierre, Joelle; Chapman, Michael; Viterbo, Domenico; Lin, Yin Yao; Mueller, Cathy M.; Chice, Seto; Schulze, Robert; Smith-Norowitz, Tamar A.; Nowakowski, Maja; Kandil, Emad; Shah, Vishal; Gross, Richard A.; Zenilman, Michael E.
CORPORATE SOURCE: Suny Downstate Med Ctr, Brooklyn, NY 11203 USA
SOURCE: FASEB Journal, (MAR 4 2005) Vol. 19, No. 4, Suppl. S, Part 1, pp. A352.
Meeting Info.: Experimental Biology 2005 Meeting/35th International Congress of Physiological Sciences. San Diego, CA, USA. March 31 -April 06, 2005. Amer Assoc Anatomists; Amer Assoc Immunologists; Amer Physiol Soc; Amer Soc Biochem & Mol Biol; Amer Soc Investigat Pathol; Amer Soc Nutr Sci; Amer Soc Pharmacol & Expt Therapeut; Int Union Physiol Sci.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 1 Dec 2005
Last Updated on STN: 1 Dec 2005

AB Introduction: We have previously demonstrated that sophorolipids decrease sepsis related mortality. In this study, we investigated changes in cell surface expression profiles of helper/cytotoxic T cells (CD4, CD8), and adhesion molecules including ICAM (CD54), L-selectin (CD62L) and integrins (CD11a, CD11b/c) on blood leukocytes obtained from sophorolipid treated septic rats, compared with untreated and sham (laparotomy) controls.Materials and Methods: Intra-abdominal sepsis was induced in rats via cecal ligation and puncture (CLP). Sophorolipids or vehicle alone were injected IV at the end of the operation. Blood leukocytes were harvested after 24 hrs and incubated with conjugated antibodies. Leukocyte subsets and expression of cell surface antigens were determined by flow cytometry.Results: Sophorolipid treated rats showed a 67% increase in lymphocyte CD11b/cexpression when compared with untreated controls ($p < 0.05$) and a trend toward decreased lymphocyte CD54 and CD62L expression. Lymphocyte CD11a expression was similar in both groups. CD4+ and CD8+ cells were 47-80% reduced in both CLP groups (+/- sophorolipid treatment) when compared with sham group ($p < 0.05$).Conclusions: Sophorolipid treatment after induction of intra-abdominal sepsis may improve survival by modulation of leukocyte adhesion molecule expression. This suggests that the integrin

O-β-D-glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate-6',6"-diacetate, Hexyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate, and Ethyl 17-L[(2'-O-β-D glucopyranosyl-β-D-glucopyranosyl)-oxy]-cis-9-octadecenoate.

5. Delivery Routes and Doses.

The sophorolipid compounds disclosed herein can be delivered in many different forms. Illustrative examples of the delivery forms include intravenous, intraarterially, and intrapreitoneal. Those of ordinary skill in the art can chose other delivery systems and formulate the novel sophorolipid into the delivery system chosen without undue experimentation.

Dosages can be determined depending on the particular sepsis or septic shock circumstance, but generally is in the 2 - 30 mg per kg of body weight range. It is contemplated that persons of ordinary skill in the art could determine an effective amount greater or less than the preferred range depending, as previously mentioned, on the particular sepsis or septic shock circumstance.

6. Combination Systems

The sophorolipids disclosed herein also can be combined in various forms and with other agents for the treatment or prophylaxis of sepsis and septic shock. For example, the sophorolipids disclosed herein can be made and/or used in combination with one or more known agent for the treatment or prophylaxis of sepsis and septic shock to produce alternative agents for the treatment or prophylaxis of sepsis and septic shock. Those of ordinary skill in the art can choose the appropriate or desired known agent for the treatment or prophylaxis of sepsis and septic shock to combine with the sophorolipids to result in an alternate agent for the treatment or prophylaxis of sepsis and septic shock without undue experimentation.

The above detailed description of the preferred embodiments, and the examples, are for illustrative purposes only and are not intended to limit the scope